REMARKS

Claims 1 and 6-11 are pending in the application. Favorable reconsideration of the application is respectfully requested in view of the amendments to the claims and following comments.

I. CLAIM REJECTIONS UNDER 35 U.S.C. §103(a)

Claims 1-4, 6 and 9-11 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Fuji et al. (WO 02/097107) in view of Suzaki et al. (Bioconversion of Cellulose to α-1,4-Glucan, 1983), Kim et al. (2002) and Nilsson (US 6,077,695). (Applicants note that claims 2-5 were previously cancelled and assume the rejection is directed to claims 1, 6 and 9-11.) The Examiner acknowledges that Fuji et al. fails to teach that cellobiose is used instead of sucrose as the raw material for producing the intermediate G1P, and that Fuji fails to teach that cellobiose phosphorylase is applied on cellobiose instead of sucrose phosphorylase on sucrose to produce G1P, and further, that Fuji fails to teach that the glucose byproduct is simultaneously removed from the solution by reaction with glucose isomerase or glucose oxidase. It is the Examiner's position that it would have been obvious based on the teachings of Suzaki et al. and Kim et al. to substitute cellobiose and CBP for sucrose and SP, respectively, to produce G1P which is then used to produce a chain extended alpha-1,4-glucan such as amylose in a coupled reaction system, as the substitution is no more than the predictable use of prior art elements according to their established functions, resulting in the simple substitution of one known element for another for a predictable result. The Examiner further contends that it would have been obvious based on the teachings of Nilsson to remove the glucose byproduct during the reaction of cellobiose and primer with CBP to make glucose and G1P wherein G1P is then used to extend an amylose chain by the action of an alpha-1,4-glucan phosphorylase. The Examiner has stated that one skilled in the art would have had a reasonable expectation that glucose isomerase could successfully prevent glucose from inhibiting CBP by converting the glucose byproduct into a non-inhibitory product.

Applicants respectfully traverse the rejection for at least the following reasons. The present invention is directed to a method for production of an α-glucan from a cellobiose, comprising coupling the reactions of:

(1) phosphorolysing a cellobiose by a cellobiose phosphorylase to produce G 1-P;

(2) reacting the G 1-P with a primer in the presence of a α-glucan phosphorylase to produce an α-glucan; and

(3) decreasing the concentration of glucose produced during reaction (1).

With regard to (3), glucose produced as a byproduct of α-glucan production is removed from the solution simultaneously as the enzymatic reactions of (1) and (2) are occurring in the same solution, and significantly the yield of α-glucan is improved about 1.4 to 2 times as compared to the reaction in which the produced glucose is not removed. Specifically, the yield of α-glucan in Example 5-1 of the present specification (not removing glucose) is 32.8%, whereas the yields of α-glucan in Examples 5-2, 5-3 and 5-4 (i.e. removing glucose) of the present specification are 45.6, 54.9 and 64.8 %, respectively (See Table 5 on page 90 of the English language specification).

In view of the combination of enzymatic reactions in the claimed method, those skilled in the art could not predict the direction of such reactions, wherein the simultaneous reactions are conducted with enzymes which share both substrate and product. Therefore, in such an unpredictable field with regard to the equilibrium and balance of enzymatic reactions it should be recognized that simply combining cellobiose phosphorylase and α-glucan phosphorylase in a single reaction solution, those skilled in the art would not necessarily have expected the desired product of α-glucan to be produced from cellobiose, or more significantly have expected the effects of improved yield of α-glucan as compared to the reaction in which the produced glucose is not removed.

It appears that the Examiner has simply combined Fuji et al. and Suzaki et al. to teach steps (1) and (2), and combined Kim et al. and Nilsson to teach the feature (3) of the claimed method, *individually*. However, the Examiner has failed to consider whether by combining the teachings of Fuji et al., Suzaki et al., Kim et al. and Nilsson,

those skilled in the art would have expected a solution wherein the reactions (1), (2) and (3) occur simultaneously to have attained the effects of the claimed method therefrom. That is, for example, after combining Kim et al. and Nilsson to assert that removing glucose as a byproduct would increase the yield of α-glucan, the Examiner failed to explain why it would have been expected that in a complicated reaction system combining two kinds of phosphorylases (i.e., as in (1) and (2) above), the reaction yield would be improved even when the byproduct is eliminated. Specifically, considering the contrasting differences and disclosure of the above prior art documents in the context of the present invention, as described below:

Kim et al.:

It is described therein that "it was concluded that D-glucose competed with G 1-P for its binding site in the synthetic reaction" in the Abstract on page 197. Thus, those skilled in the art would expect that the reduction of D-glucose would promote the reaction to proceed in the direction of cellobiose synthesis. Thus, those skilled in the art would not reduce glucose levels in order to promote the reaction for the direction of cellobiose degradation, and such disclosure teaches away from the method of the claimed invention.

Furthermore, the Examiner relies on the portion under the heading of "*Reaction Mechanism of CBP"* in left column on page 200, to assert that glucose is an inhibitor of CBP. However, such a portion does not clearly indicate which reaction of the two reactions catalyzed by CBP, (i.e., phosphorolytic and synthetic reactions) is inhibited, wherein as described in the abstract lines 2-3 of Kim et al., CBP catalyzes these two reactions.

Under the heading of "*Substrate Specificities in the Synthetic Reaction*" at the bottom of left column on page 200, it is recited that "Among them, the strongest inhibition was observed with D-glucose" on line 14, right column of page 200, referring to that when a synthetic reaction (which is a reverse reaction of phosphorolytic reaction) proceeds, glucose inhibits the synthetic reaction.

Under the heading "*Inhibition Mechanism of D-Glucose"* on left column of page 201, there is a description that "A remarkable decrease in the initial velocity of the

reverse reaction was detected with an increase in the concentration of D-glucose". This means that if the glucose concentration of reaction is increased, the initial velocity of the reverse reaction, i.e., synthetic reaction, decrease, i.e., the synthetic reaction is inhibited.

To summarize, from the above descriptions in Kim et al., those skilled in the art would expect that if the glucose concentration of the reaction is decreased, then the reverse reaction, (i.e., synthetic reaction), would proceed advantageously and synthesize of amylose yield would decrease, thus, Kim et al. does not describe or suggest that removal of glucose would increase the yield of the amylose synthesized by the present invention.

Nilsson:

Describes a transglycosylation reaction using a glucosyl enzyme, and thus in contrast to the present invention, both a different enzymatic reaction and enzyme are used therein.

In support of Applicants' position, Applicants point out that in Reference Example 2 on page 94, line 28 to page 96, line 5 of the English language specification of the present application, it is demonstrated that in the reaction system in which sucrose is produced from cellobiose, by removing glucose from the reaction system, the yield of sucrose was not improved significantly.

The method of the present invention is directed to the development of a low cost, simple and effective method for performing a reaction in a single reaction system by coupling of enzymes, in order to produce a significant yield of α-glucan from cellobiose. The combined teachings of Fuji et al., Suzaki et al., Kim et al. and Nilsson fail to address (i) the problem to be solved by the method of the present invention, (ii) the claimed mechanism to arrive at the solution, and (iii) the effects obtained therefrom.

In view of the foregoing comments, it is apparent that those skilled in the art would not have expected to have succeeded in achieving the claimed method and expected the significant α-glucan yields therefrom, based on the combined teachings of Fuji et al., Suzaki et al., Kim et al. and Nilsson. Because prima facie obviousness has

not been established, the rejection of claims 1, 6 and 9-11 under 35 U.S.C. §103(a) should be withdrawn.

Claims 1-4, and 6-11 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Fuji et al. (WO 02/097107) in view of Suzaki et al. (Bioconversion of Cellulose to α-1,4-Glucan, 1983), Kim et al. (2002), Wada et al. (JP 2003093090; machine translation) and Taguchi et al. (1994, abstract only). (Applicants note that claims 2-5 were previously cancelled and assume the rejection is directed to claims 1 and 6-11.) The Examiner states that the combined teachings of Fuji et al. and Suzaki et al. fail to disclose that the glucose byproduct is removed from the solution by simultaneous reaction with glucose oxidase, mutarotase and catalase (claims 6-8). It is the Examiner's position that it would have been obvious to employ a system comprising glucose oxidase, mutarotase and catalase to eliminate the glucose byproduct in a reaction system that converts cellobiose and primer to G1P and glucose wherein the G1P is used to extend the chain of amylose by the action of alpha-1,4-glucan phosphorylase, as the ordinary artisan would have had a reasonable expectation that the trio of enzymes would successfully eliminate unwanted glucose byproduct based on the teachings of Taguchi et al.

Applicants respectfully traverse the rejection for at least the following reasons. As discussed above, the present invention is directed to a method for production of an α-glucan from a cellobiose, comprising coupling the reactions of:

(1) phosphorolysing a cellobiose by a cellobiose phosphorylase to produce G 1-P;

(2) reacting the G 1-P with a primer in the presence of a α-glucan phosphorylase to produce an α-glucan; and

(3) decreasing the concentration of glucose produced during reaction (1).

It appears that the Examiner has simply combined Fuji et al. and Suzaki et al. to teach steps (1) and (2), and combined Kim et al., Wada et al. and Taguchi et al. to teach the feature (3) of the claimed method, *individually*. However, the Examiner has failed to consider whether by combining the teachings of Fuji et al., Suzaki et al., Kim et

al., Wada et al. and Taguchi et al., those skilled in the art would have expected a solution wherein the reactions (1), (2) and (3) occur simultaneously to have attained the effects of the claimed method therefrom. That is, for example, after combining Kim et al., Wada et al. and Taguchi et al. to assert that removing glucose as a byproduct would increase the yield of α-glucan, the Examiner failed to explain why it would have been expected that in a complicated reaction system combining two kinds of phosphorylases (i.e., as in (1) and (2) above), the reaction yield would be improved even when the byproduct is eliminated. Specifically, considering the contrasting differences and disclosure of the above prior art documents in the context of the present invention, as described below:

Kim et al.:

(Discussed above)

Wada et al.:

It is disclosed that the yield of inulin is increased by removing glucose. However, as described in Table 1 of Wada et al, the yield was improved only about 2% (yield is 45.1% for no addition and 47.2% for addition). Compared with this stated improvement, the improvement obtained by the present invention is unexpectedly significant. Furthermore, both a different enzymatic reaction and enzyme are used therein.

Taguchi et al.:

This reference discloses the elimination of blood glucose that interferes with the enzymatic determination of 1, 5-anhydroglucitol. In this method, 1,5-anhydroglucitol is oxidized by using glucose-2-oxidase to generate hydrogen peroxide. If the blood contains glucose, the glucose is also oxidized into hydrogen peroxide by glucose-2-oxidase. Thus, the elimination of blood glucose is needed in an accurate measurement of 1,5-anhydroglucitol. As such, the glucose itself does not interfere with the enzymatic reaction, but interferes with the measurement of the byproduct of hydrogen peroxide, and thus it is neither described nor suggested that the enzyme reaction is inhibited by glucose.

The method of the present invention is directed to the development of a low cost, simple and effective method for performing a reaction in a single reaction system by coupling of enzymes, in order to produce a significant yield of α-glucan from cellobiose.

The combined teachings of Fuji et al., Suzaki et al., Kim et al., Wada et al. and Taguchi et al. fail to address (i) the problem to be solved by the method of the present invention, (ii) the claimed mechanism to arrive at the solution, and (iii) the effects obtained therefrom.

In view of the foregoing comments, it is apparent that those skilled in the art would not have expected to have succeeded in achieving the claimed method and expected the significant α-glucan yields therefrom, based on the combined teachings of Fuji et al., Suzaki et al., Kim et al., Wada et al. and Taguchi et al.. Because prima facie obviousness has not been established, the rejection of claims 1, 6-11 under 35 U.S.C. §103(a) should be withdrawn.

II. CONCLUSION

Accordingly, claims 1 and 6-11 are believed to be allowable and the application is believed to be in condition for allowance. A prompt action to such end is earnestly solicited.

Should the Examiner feel that a telephone interview would be helpful to facilitate favorable prosecution of the above-identified application, the Examiner is invited to contact the undersigned at the telephone number provided below.

Should a petition for an extension of time be necessary for the timely reply to the outstanding Office Action (or if such a petition has been made and an additional extension is necessary), petition is hereby made and the Commissioner is authorized to charge any fees (including additional claim fees) to Deposit Account No. 18-0988.

Respectfully submitted,

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